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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/265,606	03/10/1999	RAINER ZIMMERMANN	LUD5330.3DIV	4727

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/265,606	ZIMMERMANN ET AL.	
	Examin r	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Reopen Prosecution

In view of the Appeal Brief filed on 6/4/03, PROSECUTION IS HEREBY REOPENED. See the new grounds of rejection set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Applicant's arguments with respect to the pending claims set forth in the Appeal Brief have been considered but are moot in view of the new ground(s) of rejection set forth below. All rejections and objections not reiterated below are hereby withdrawn.

Election/Restrictions

In view of the fact that the search for claims 20 and 22-26 is co-extensive with a search for claim 20, the restriction requirement is hereby withdrawn. Claims 20-26 are pending and are considered elected.

Priority

The instant application claims priority to two previous applications. Application 08/230,491, filed April 20, 1994 provides no disclosure anywhere of a fusion or chimeric protein comprising "portions" of a non- FAPα, and therefore does not provide support for instant claims 20-21 and 23-26. Application 08/230,491 does disclose sequences, in Table 2, identical to instant SEQ ID NO's 4,6, and 7, and thus provides written description support for claim 22. However, the disclosure of 08/230,491 does not enable the subject matter of instant claim 22 for the same reasons as those set forth below for the instant application. For these reasons, priority is not granted to 08/230,491 for any pending claim.

The specification of Application 08/940,391 is identical to that of the instant specification, and therefore provides written description support for all of the pending claims. However, as partial enablement of claims 20-21 and 23-26 depends on the teachings of NIEDERMEYER, published June, 1998 (see below), the disclosure of 08/940,391 is not enabling for instant claims 20-21 and 23-26. Further, claim 22 is not enabled by the instant disclosure or the teachings of the prior art, as set forth below. For these reasons, priority is not granted to 08/940,391 for any pending claim.

For the reasons set forth above, the priority of the pending claim is granted only to the filing date of the instant application, of 3/10/1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

Claims 20-21 and 23-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein comprising an extracellular domain of FAPα, does not reasonably provide enablement for a fusion or chimeric protein comprising any smaller portion of FAPα, specifically for a fusion or chimeric protein comprising any one or a combination of SEQ ID NO's 4, 6, and/or 7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

Claims 20-21 and 23-26 are enabled for an isolated protein comprising an extracellular domain of FAPα because the prior art teaches how to make such a protein and both the specification and prior art teach how use such a protein. Specifically, the specification provides guidance on pages 21-22 that a fusion protein comprising the

extracellular domains of both FAPα and murine CD8 exhibits catalytic activity, therefore one skilled in the art would know how to use a fusion protein comprising the entire extracellular domain of FAPα. However, the specification does not disclose what residues (i.e. by reference to amino acid numbering, a SEQ ID NO, etc.) of FAPα was used to construct the fusion protein of pages 21-22. The specification, on page 11, discloses that a "hydrophobic, transmembrane domain is double underlined" in Figure 1. Figure 1 shows SEQ ID NO: 1 (the sequence of the inventive FAPα protein) aligned with a CD26 sequence; however, no portion of either protein is double underlined. There are no markings on Figure 1 anywhere which appear to identify any particular domain of FAPα . The specification also discloses, on page 12, that the FAPα molecule comprises a large COOH-terminal extracellular domain, a hydrophobic transmembrane segment, and a short cytoplasmic tail. If Figure 1 indeed identified a transmembrane domain, then given the disclosure of page 12, it would be fairly simple to determine which residues constitute the extracellular domain used in making the fusion protein comprising catalytic activity on pages 21-22. However, in the absence of any disclosure identifying residues of either the extracellular domain or the transmembrane domain, one skilled in the art would have to guess which residues comprise the "relatively large extracellular domain", and therefore would not know how to make a fusion protein comprising this domain. For these reasons, the specification alone is not enabling for how to make the claimed protein. It is noted, however, that NIEDERMEYER et al. (European Journal of Biochemistry (June 1998) Volume 254 (2), pp. 650-654) teaches how to make fusion proteins comprising either a mouse or a human cytoplasmic domain

of a FAPα protein, and specifically teaches that cytoplasmic domain of the human protein consists of amino acids 27-760 (p. 652, right column). NIEDERMEYER also teaches that his constructs have catalytic activity (p. 653, Fig. 4), thus teaching both how to make and use a fusion protein comprising an extracellular domain of FAPα and an extracellular CD8 fragment. It is noted that the disclosure of priority application 08/940,391 is identical to that of the instant specification. However, as NIEDERMEYER was published after the filing date of the priority application, and the disclosure alone is not enabling for claims 20-21 and 23-26, the instant claims were not enabled as of the filing date of 08/940,391.

Claims 20-21 and 23-26 are not enabled for a fusion or chimeric protein comprising any portion of FAPα less than the entire extracellular domain because neither the prior art nor the specification teach how to use a fusion protein comprising any portion of FAPα which consists of less than the entire extracellular domain. Claim 22 is not enabled because neither the specification nor the prior art teach how to use an isolated peptide consisting of SEQ I DNO: 4 or SEQ ID NO: 6 or SEQ ID NO: 7.

The scope of claims 20-21 and 23-26 is broad as they embody a fusion protein comprising any one of the recited SEQ ID NO's or some combination of the recited SEQ ID NO's, and any fragment of SEQ ID NO: 1 up to the entire length of SEQ ID NO: 1. The scope of claim 22 is narrower than claims 20-21 and 23-26 as it is limited to one of three specific SEQ ID NO's. The state of the prior art is such that the entirety of FAPα is known as are fusion proteins comprising the entire extracellular domain (see NIEDERMEYER et al., supra).

With regard to claim 22 and embodiments of a fusion protein comprising a catalytic domain which consists of SEQ ID NO: 4, 6, or 7, the specification provides guidance on page 12 that the extracellular domain of FAPα contains three segments corresponding to highly conserved catalytic domains characteristic of serine proteases. The specification provides further guidance on page 13, in Table 2, that a putative catalytic domain of FAPα comprises at least residues 621-737 and *all three* of the recited SEQ ID NO's. The prior art of NIEDERMEYER confirms that human FAPα comprises a catalytic triad and at least one catalytic consensus motif (p. 652). Neither the specification nor the prior art, however, teach whether any of SEQ ID NO's 4, 6, or 7, alone, have catalytic activity, or would be expected to have catalytic activity in a fusion protein. The prior art teaches that consensus motifs of catalytic domains in DPPIV and FAPα are similar to each other and different from those of classical serine proteases. See NIEDERMEYER (supra, p. 652) and OGATA et al. (Biochem. (1992) vol. 31, pp. 2582-2587), at page 2583. Thus, there is a degree of uncertainty in the art as to whether teachings with regard to classical serine proteases would apply to DPPIV and FAPα . The prior art of OGATA teaches that particular residues are necessary for catalytic activity in DPPIV (p. 2585), but does not teach whether any single amino acid or domain is sufficient for such activity. Neither the prior art nor the instant specification teach whether any single domain of either DPPIV or FAPα , as an isolated peptide, has catalytic activity. Nor does the prior art or specification teach whether an isolated domain of FAPα , as represented by SEQ ID NO: 4, 6, or 7, or combination of single domains, wherein the domain(s) is/are NOT in the environment of the entire

extracellular domain, in combination with an exogenous peptide sequence in a fusion protein, has catalytic activity.

The degree of skill in the art is acknowledged to be high, however, given the uncertainty in the art and the lack of teaching in either the specification or the prior art for whether isolated catalytic domains of FAPα would have catalytic activity or would have activity in a fusion protein, it would require undue experimentation for one skilled in the art to determine how to use an isolated peptide consisting of SEQ ID NO: 4, 6 or 7. For the same reasons, it would require undue experimentation for one skilled in the art to determine how to use a fusion or chimeric protein comprising any one or a combination of SEQ ID NO's 4, 6 or 7 wherein those sequences are not comprised within the entirety of an extracellular domain of FAPα.

For all of the reasons set forth above, claim 22 is not enabled, and claims 20-21 and 23-26 are enabled only for a protein comprising the extracellular domain of FAPα.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-21, 23, and 25-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites "at least one portion of a non FAPα protein" in step (ii). The specification sets forth definitions of non FAPα proteins, as previously argued, but does

not specifically define what is meant by "at least one portion" of a non FAPα protein. It is noted that a "portion" may be a single amino acid. As FAPα comprises all 20 normal amino acids, then it is unclear whether that "portion" is indeed one of a "non FAPα protein". As it is unclear what limitation is intended by a "portion of a non FAPα protein", the claims are indefinite. Applicant is reminded that claim 24, which specifically defines the "at least one portion of a non FAPα protein" is not rejected herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 20-21 and 23-26 are rejected under 35 U.S.C. 102(a) as being anticipated by NIEDERMEYER et al. (European Journal of Biochemistry (June 1998) Volume 254 (2), pp. 650-654).

NIEDERMEYER teaches fusion/chimeric proteins comprising the extracellular domain of human FAPα and the extracellular fragment of CD8 (p. 652, right column). The sequence of human FAPα is identical to instant SEQ ID NO: 1, and NIEDERMEYER teaches that his extracellular domain consists of amino acids 27-760, and has catalytic activity, thus NIEDERMEYER's protein inherently comprises at least

one catalytic domain consisting of a sequence identical to SEQ ID NO: 4, 6 and 7, and anticipates claims 20-21 and 23-26.

Conclusion

Claims 20-26 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

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Marjorie A. Moran
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